



# AEC-NASA TECH BRIEF



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## Microscopes and Computers Combined for Analysis of Chromosomes

### The problem:

To obtain quantitative information on chromosome analysis. Cytological techniques for chromosome analysis have revealed evidence that many specific chromosome disorders in man are correlated with definite diseases or anomalies. Accumulation of this evidence is long and tedious, however, because of the manual methods being used. Newer and more rapid techniques are needed for recognizing small, but genetically important, abnormalities of chromosomes not easily detected using normal microscopic techniques.

### The solution:

A scanning machine (CHLOE), developed for the automatic analysis of photographic material, has been adapted for use in the analysis of chromosomes. This machine has been combined with a digital computer to obtain quantitative and statistically significant data on chromosome shapes, distribution, density, and pairing.

On analysis of the computer pairing versus human pairing, the computer, with good quality input film, was more efficient and faster than man in selecting the correct chromosome pairs. With this present setup, it is possible to obtain statistical information about a chromosome complement (46 chromosomes) two thousand times faster than is possible by manual pairing.

### How it's done:

Basically, the method requires that the metaphase spreads of the chromosomes to be scanned be photographed on 35-mm film and read either horizontally or vertically. The numerical data derived from the scan are recorded by CHLOE's associated computer, the ASI-210, which registers the data and records the results on magnetic tape. The magnetic tape is then fed into the CDC-3600 computer which completes the

analysis of the data and reconstitutes the chromosomes, and, finally, pairs the chromosomes with their homologues.

The input for the CHLOE system consists of a full complement of chromosomes, photographed on 35-mm film. The chromosomes are first prepared and fixed, spread apart on a microscope slide, and stained, usually with Giemsa. The photographing is performed with a Leica camera attached to an astrophoto Zeiss microscope with a 63X Planachromat objective or with a 100X Neofluar oil emulsion objective.

The system for automated measurements and classification of the chromosomes consists of several units. The ASI-210 computer is the principal control and information processing unit. The scanner, CHLOE, consists of a cathode ray tube and a photomultiplier (with the film to be scanned stretched between the units). During the actual scanning of a metaphase spread, a spot of light from the CRT is projected onto the film, and the light transmitted through the film is registered by the photomultiplier. The spot of light is controlled by two digital counters, and appears in one place for 1  $\mu$ sec, is cut off for 4  $\mu$ sec, and reappears in an adjacent location for 1  $\mu$ sec.

When the photomultiplier detects a measurable change in the transmitted light from one edge coordinate of a chromosome to the other, the contents of the counters are sent into the computer memory as the coordinates of the point. This information is stored as horizontal line segments. About 30 to 100 line segments are read for each chromosome and each segment is labeled with a number. The labeled segments are then written out on a magnetic tape for use as input to the CDC-3600 computer, which has been programmed to reconstruct these segments into chromosome shapes using Euclidean moment invariants.

(continued overleaf)

The chromosome-pairing is performed by the same CDC-3600 program, after reconstruction of the chromosomes from the original digital data.

**Notes:**

1. This technique would be useful for expediting the accumulation and evaluation of chromosome data, and may thus be of interest to persons concerned with biochemical analysis.
2. Additional information is contained in "The Microscope," Vol. 15, Third Quarter, July 1967, pp. 68-77.
3. Inquiries concerning this innovation may be directed to:

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**Patent status:**

Inquiries about obtaining rights for commercial use of this innovation may be made to:

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